

# G IDS-iSYS InaKtif MGP (dp-ucMGP) CKD-MBD

An automated assay for the quantitative determination of the inactive dephosphorylated-uncarboxylated (dp-uc) isoform of Matrix Gla-Protein (MGP) in human plasma. Measurement of dp-ucMGP are used the assessment of vitamin K status in the arterial vessel wall.

Matrix Gla-Protein (MGP) is the most potent inhibitor of tissue calcification presently known. MGP is a **y**-carboxylated 11 kDa protein, comprised of 84 amino acids, which is mainly expressed and secreted by chondrocytes and vascular smooth muscle cells in the arterial media.<sup>1</sup> Vitamin K serves as a co-factor for the enzyme **y**-glutamate carboxylase that converts glutamate residues into **y**-carboxyglutamate (Gla). These Gla-residues serve as calcium-binding groups, which are essential for the activity of all Gla-containing proteins including MGP. Besides carboxylation, MGP also undergoes post-translational serine phosphorylation during maturation. Whereas carboxylation is essential for its calcification inhibitory activity, its cellular secretion is enhanced by phosphorylation.<sup>2,3</sup> At least four different MGP species are formed with varying states of phosphorylation and/or carboxylation: phosphorylated carboxylated MGP (p-cGMP), phosphorylated uncarboxylated MGP (p-ucMGP), desphospho-carboxylated MGP (dp-cMGP), and desphospho-uncarboxylated MGP (dp-ucMGP). Circulating forms of MGP have no known biological function, but reflect the extent of vascular calcification and availability of Vitamin K in the vessel wall.<sup>2,4,5</sup>

Large evidences from last two decades indicate the disturbances in mineral and bone metabolism in chronic kidney disease patients (CKD) link with vascular calcification (VC). VC is associated with increased cardiovascular mortality and morbidity, and is recognized as a strong and independent risk factor for cardiovascular death. Various studies described a decreased availability of vitamin K, both K1 and K2, in CKD patients. Vitamin K therapy has been shown to significantly decrease the levels of dp-ucMGP both in the general population and haemodialysis patient. Conversely, it has been documented that vitamin K antagonist (VKA) is associated with higher dp-ucMGP levels.

Vitamin K status can be assessed in two different ways: (i) by measuring vitamin K concentration in plasma or (ii) by determining the amount of inactive vitamin K-dependent proteins. The first method reflects a snapshot and is influenced by triglyceride concentrations and recent vitamin K intake. The circulating vitamin K levels give little information about the vitamin K utilization in tissue. To determine the vitamin K status in the arterial vessel wall, it is better to measure the dp-ucMGP levels.

# Features and benefits

- Utilise conformation-specific monoclonal antibodies to ensure accurate dp-ucMGP circulating levels
- Correlated to the widely published lab-developed dp-ucMGP ELISA assay method
- Wide assay range suitable for Chronic Kidney Disease, Haemodialysis and Vitamin K Antagonist treated patients
- First fully automated CE marked IVD dp-ucMGP test for achieving fast and highly reproducible results for diagnostic and follow up of patients

### Commitment to innovation

## **Specifications**

Format	Automated chemiluminescen	ce sandwich immunoassau			
Calibrators	Luaphilized Desch of Descentration levels 1.0 ml				
					• • •
Controls	Lyophilised – 3 each of 3 conc	entration levels, 1.0 mL			
Limit of Quantitation	300 pmol/L				
Dynamic range	300 – 12,000 pmol/L				
Minimum Sample Volume	50 μL plus dead volume				
Sample Type	Human plasma – collected in potassium EDTA tube				
Reagent Stability	The IDS-iSYS InaKtif MGP reagent cartridge may be stored after opening on-board the IDS-iSYS Multi Discipline Auto- mated System for up to 14 days or at 2–8°C for up to 28 days				
Calibration Stability	The calibration of the IDS-iSYS InaKtif MGP assay is stable for up to 14 days				
Time to First Result	64 minutes				• • •
Precision	Sample ID	Mean (pmol/mL)	Within Run %CV	Total %CV	
	1	591	4.5	7.9	
	2	870	6.2	8.2	
	3	2,558	0.8	3.5	
	4	4,067	1.1	3.4	
	5	6,488	0.8	3.3	

#### Method Comparison



The IDS-iSYS InaKtif MGP assay was compared against a VitaK lab developed dp-ucMGP ELISA method, following CLSI EP-9A2, "Method Comparison and Bias Estimation Using Patient Samples". A total of 122 samples, selected to represent a wide range of dp-ucMGP concentrations [311 – 5,376 pmol/L], was assayed by each method. Linear regression analysis was performed on the comparative data:

Slope		Intercept (pmol/L)		Correlation
95% Cl		95% Cl		coef. (r)
0.83	0.80 to 0.86	93.1	40.4 to 145.8	0.98

#### **Complementary Products**

G	Product Name	Code	
IDS-iSYS 25 VitDs		IS-2500	
IDS-i	IS-2400		
IDS-iSYS 1,25 VitD <sup>xp*</sup>		IS-2000	
IDS-iSYS Intact PTH		IS-3200	
IDS-iSYS Ostase® BAP		IS-2800	
IDS-iSYS Intact PINP		IS-4000	
IDS-iSYS TRAcP 5b (BoneTRAP®)*		IS-4100	

\*Available in selected markets.

Product availability subject to regulatory approval.

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1. Price PA, Urist MR, Otawara Y: Matrix Gla protein, a new gammacarboxyglutamic acid-containing protein which is associated with the organic matrix of bone. Biochem Biophys Res Commun 1983, 117:765–771. 2. Cranenburg EC, Koos R, Schurgers LJ, Magdeleyns EJ, Schoonbrood TH, Landewé RB et al. Characterisation and potential diagnostic value of circulating matrix Gla protein (MGP) species. Thromb Haemost. 2010; 104: 811–822. 3. Schurgers LJ, Spronk HM, Skepper JN, Hackeng TM, Shanahan CM, Vermeer C et al. Post-translational modifications regulate matrix Gla protein function: importance for inhibition of vascular smooth muscle cell calcification. J Thromb Haemost. 2007; 5: 2503–2511. 4. Murshed M, Schinke T, McKee MD et al. Extracellular matrix mineralization is regulated locally; different roles of two gla-containing proteins. J Cell Biol 2004; 165:625-630. 5. Schurgers LJ, Cranenburg EC, Vermeer C. Matrix Gla-protein: the calcification inhibitor in need of vitamin K. Thromb Haemost. 2008; 100: 593–603.

Code

ML3004 Version 1.0



# Product Name

Ordering information

IDS-iSYS Ina <i>K</i> tif MGP (dp-u-MGP)	Reagent pack: 100 tests	IS-4700
IDS-iSYS InaKtif MGP (dp-u-MGP)	Control set: 3 levels	IS-4730
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Description

Visit www.idsplc.com for an extended range of IDS-iSYS assays

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